Théo Willeman*, Justine Grunwald, Marc Manceau, Frédéric Lapierre, Lila Krebs-Drouot, Coralie Boudin, Virginie Scolan, Hélène Eysseric-Guerin, Françoise Stanke-Labesque and Bruno Revol

Smartphone swabs as an emerging tool for toxicology testing: a proof-of-concept study in a nightclub

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Abstract

Objectives: Smartphones have become everyday objects on which the accumulation of fingerprints is significant. In addition, a large proportion of the population regularly uses a smartphone, especially younger people. The objective of this study was to evaluate smartphones as a new matrix for toxico-epidemiology.

Methods: This study was conducted during two separate events (techno and trance) at an electronic music nightclub in Grenoble, France. Data on reported drug use and whether drugs were snorted directly from the surface of the smartphone were collected using an anonymous questionnaire completed voluntarily by drug users. Then, a dry swab was rubbed for 20 s on all sides of the smartphone. The extract was analyzed by liquid chromatography coupled to tandem mass spectrometry on a Xevo TQ-XS system (Waters).

Results: In total, 122 swabs from 122 drug users were collected. The three main drugs identified were MDMA (n=83), cocaine (n=59), and THC (n=51). Based on declarative data, sensitivity ranged from 73 to 97.2 % and specificity from 71.8 to 88.1 % for MDMA, cocaine, and THC. Other substances were identified such as cocaine adulterants, ketamine, amphetamine, LSD, methamphetamine, CBD, DMT, heroin, mescaline, and several NPS. Numerous medications were also identified, such as antidepressants, anxiolytics, hypnotics, and painkillers. Different use patterns were identified between the two events.

Conclusions: This proof-of-concept study on 122 subjects shows that smartphone swab analysis could provide a useful and complementary tool for drug testing, especially for harm-reduction programs and toxico-epidemiolgy studies, with acceptable test performance, despite declarative data.

Keywords: smartphones; toxico-epidemiology; recreational drugs; new psychoactive substances

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***Corresponding author: Théo Willeman**, Laboratoire de Pharmacologie, Pharmacogénétique et Toxicologie, CHU Grenoble Alpes, Institut de Biologie et de Pathologie, Univ Grenoble Alpes, CS 10217, 38043 Grenoble cedex 9, Grenoble, France; and Clinique de Médecine Légale, CHU Grenoble Alpes, Univ Grenoble Alpes, Grenoble, France, E-mail: twilleman@chu-grenoble.fr. https://orcid.org/0000-0002-0348-7171

Justine Grunwald, Laboratoire de Pharmacologie, Pharmacogénétique et Toxicologie, CHU Grenoble Alpes, Institut de Biologie et de Pathologie, Univ Grenoble Alpes, Grenoble, France; and CEIP-Addictovigilance, CHU Grenoble Alpes, Univ Grenoble Alpes, Grenoble, France

Marc Manceau, Clinical Research Center, Inserm CIC1406, Grenoble Alpes University Hospital, Grenoble, France

Frédéric Lapierre, La Belle Electrique Nightclub, Grenoble, France

Lila Krebs-Drouot, Clinique de Médecine Légale, CHU Grenoble Alpes, Univ Grenoble Alpes, Grenoble, France

Coralie Boudin, Laboratoire de Médecine Légale, Univ Grenoble Alpes, Grenoble, France

Virginie Scolan, Clinique de Médecine Légale, CHU Grenoble Alpes, Univ Grenoble Alpes, Grenoble, France; and Laboratoire de Médecine Légale, Univ Grenoble Alpes, Grenoble, France

Hélène Eysseric-Guerin, Laboratoire de Pharmacologie, Pharmacogénétique et Toxicologie, CHU Grenoble Alpes, Institut de Biologie et de Pathologie, Univ Grenoble Alpes, Grenoble, France; and Laboratoire de Médecine Légale, Univ Grenoble Alpes, Grenoble, France

Françoise Stanke-Labesque, Laboratoire de Pharmacologie, Pharmacogénétique et Toxicologie, CHU Grenoble Alpes, Institut de Biologie et de Pathologie, Univ Grenoble Alpes, Grenoble, France; and Laboratoire HP2 Inserm U1300, Univ Grenoble Alpes, Grenoble, France

Bruno Revol, CEIP-Addictovigilance, CHU Grenoble Alpes, Univ Grenoble Alpes, Grenoble, France; and Laboratoire HP2 Inserm U1300, Univ Grenoble Alpes, Grenoble, France

Introduction

Fingerprints consist of a mixture of sweat and sebum on the papillary ridges of the fingers. In forensic sciences, fingerprint analysis has long been recognized as an essential tool for identification purposes. However, recent advances in analytical techniques have expanded the utility of fingerprints, enabling the detection and profiling of various chemical substances of forensic interest, such as illicit drugs [1]. Indeed, medications present in the blood reach the

surface of the skin through sebum and sweat [2]. For example, the detection of cocaine, opiates, amphetamines, tetrahydrocannabinol, and mephedrone has been shown to be possible [3, 4]. The excretion of xenobiotics through sweat is dynamic over time and the detection window can be longer for several drugs, such as acetaminophen and dihydrocodeine, in fingerprints than in conventional matrices (blood, urine, saliva) [5].

Recently, fingerprints transferred to manipulated objects were evaluated for nicotine and codeine in two controlled studies [6]. Fingerprints have also been studied for noninvasive therapeutic drug monitoring of isoniazid [7]. The main limitations of this approach are likely to be environmental contamination and the secondary transfer of drugs, and the determination of thresholds is necessary, particularly for drugs of abuse [8, 9].

Smartphones have become an everyday personal device for a large proportion of the population, especially younger people, on which the accumulation of fingerprints is significant. The number of mobile network subscriptions for smartphones worldwide reached nearly 6.6 billion by 2022 and is expected to exceed 7.8 billion by 2028 [10]. Smartphones could, therefore, represent a new matrix for forensic toxicology. This matrix has been evaluated for drug detection with satisfactory results, except for acidic or neutral drugs [11] and individual profiling [12].

The research methods and tools used to collect data for monitoring purposes require constant evolution due to the changing nature of the drug-use situation [13]. Drug consumption monitoring can combine multiple sources of data, including data with and without toxicological analysis. Indeed, wastewater analysis, drug checking at festivals, toxicological analysis for intoxicated patients, driving under the influence (DUID) analysis, hair analysis, breath analysis, and post-mortem cases represent valuable sources of data [13–18]. Declarative data, including social media and online forums, surveys, and targeted questionnaires in community-based organizations can be useful as well [19–21].

The objective of this study was to evaluate smartphone swabs as a tool for toxico-epidemiology in a real-life setting.

Materials and methods

Sample and data collection

This study was conducted at two separate events (techno and trance) in an electronic music nightclub in February 2023 in Grenoble, France. Communication of the study was based on flyers distributed inside the nightclub during both events, without any coverage on social media. Participation was anonymous and free. The inclusion criteria were as follows: participant aged over 18 who reported the use of psychoactive substances in the last seven days who owned a smartphone. The exclusion criteria was an objection to the use of their data. A table for smartphone sampling and participant data collection was installed next to a harm reduction program booth held by an association. An anonymous questionnaire was completed by drug users to gather information on drug use and whether the drugs were snorted directly from the surface of the smartphone.

Chemicals and reagents

Invasive sterile EUROTUBO® collection swabs were purchased from Deltalab (Barcelona Spain). LC–MS acetonitrile was purchased from VWR (Leuven, Belgium). Ultrapure water with a resistivity ≥18.0 MΩ cm was produced using a Milli-Q Plus® system (Millipore, Molsheim, France). Other chemicals used were purchased from Carlo Erba reagents (Val-de-Reuil, France) or VWR (Leuven, Belgium). Deuterated internal standards (metformine-d6, haloperidol-d4, methadone-d3, diazepam-d5) were purchased from LGC Standards (Luckenwalde, Germany).

Sample preparation

The analytical method has been previously described [11]. Briefly, each smartphone was rubbed for 20 s on all sides. Then, swabs were stored at room temperature and protected from light until analysis. The cotton tip from the swab was cut from the wooden stick and incubated in 1 mL methanol (with 1 µL 2.5 mg/L IS mix) for 10 min on a rocking shaker and then evaporated to dryness under a stream of nitrogen. The dry residue was reconstituted in 100 µL aqueous phase A (5 mM ammonium formate and 0.1 % formic acid). The sample was then ready to be injected into the chromatographic system.

UPLC-MS/MS method

Ultrahigh performance liquid chromatography (UPLC) was performed on an I-class Acquity system (Waters Milford, USA). Chromatographic separation was achieved using an Acquity HSS T3 column (100 mm × 2.1 mm, 2.5 µm) (Waters). Mobile phase A consisted of 5 mM ammonium formate and 0.1 % formic acid and mobile phase B of ACN with 0.1 % formic acid. A gradient program was set as follows: 0–0.5 min: 13 % B, 0.5–10 min: 13–50 % B, 10–10.75 min: 50–95 % B, 10.75–12.25 min: 95 % B, 12.25–12.5 min: 95–13 % B, 12.5–15 min: 13 % B. An analytical run lasted 15 min. The flow rate of the mobile phase was 0.4 mL/min. The oven temperature was set to 40 °C and the injection volume was 5 µL for each targeted screening.

Qualitative targeted screenings were performed on a Xevo TQ-XS (Waters) tandem mass spectrometer by positive and negative electrospray ionization (ESI) in the scheduled multiple reaction monitoring (MRM) mode. The following conditions were used for the analysis: capillary voltage of 0.5 kV, source temperature of 150 °C, desolvation temperature of 650 °C, cone gas flow rate of 150 L/h, and desolvation gas flow rate of 900 L/h. The cone voltage and collision energy were optimized for each compound. The acquisition consisted of two separate scheduled MRM targeted screenings: one included 349 drugs and one included 166 NPS, containing two MRM transitions, except for tramadol and the internal standards (metformine-d6, haloperidol-d4, methadone-d3, and diazepam-d5) with one MRM transition.

Isomer characterization, such as isomers of methylmethcatinone, was not possible with this chromatographic method. They are named X-MMC and X-CMC in this paper.

Identification criteria were the presence of two MRM transitions, a signal/noise ratio >3, a transition ion ratio accuracy <40 %, and a retention time accuracy <0.2 min. This qualitative targeted screening by UPLC-MS/MS is routinely used in our laboratory for clinical and forensic samples in conventional matrices (whole blood, plasma, and urine) and has been validated according to the SFTA-SFBC guidelines [22]. Proficiency testing programs from SFTA and ProBioQual® ensured the quality of the screening. Data were analyzed using MassLynx (v4.2, Waters). The list of positive identifications with the *m*/*z* transitions, retention times, and ion ratios are detailed in Supplementary Table S1.

Data analysis

For evaluation of the performance of the smartphone swab protocol, we compared the results with the declaration of the participants for cocaine, MDMA, THC, ketamine, and LSD. The following parameters were calculated using Jamovi software v1.4 [23]: sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The formulas were as follows: sensitivity=TP/(TP + FN), specificity=TN/(TN + FP), PPV=TP/(TP + FP), NPV=TN/(FN + TN), with TP as true positive, FP as false positive, FN as false negative, and TN as true negative.

Networks were built and plotted using R software and the ggraph module. Nodes represent substances and edges linking two nodes represent the number of smartphones positive for the two associated substances.

Ethics

This project is a research project that does not involve the human being and whose controller is the Centre Hospitalier Grenoble-Alpes. This research has been registered in accordance with French regulations and meets the requirements of the CNIL reference methodology.

Results

Drug identifications and consumption patterns

This study included 122 swabs from 122 drug users, 61 each night. There were 1,000 people each night at the nightclub. Thus, sampling represented 6.1 % of the attendees. The acceptation of the project by and feedback from the participants were satisfying.

The identification of the substances, as well as the consumption patterns per night, are presented in Table 1. Only one swab revealed no substances, even though the participant reported cannabis and LSD consumption. Eighteen percent of participants had used drugs directly on their smartphone. Polydrug use was more common during the trance night, with 12 participants reporting three or more substances. MDMA and cocaine were the most highly detected substances at the techno and trance nights, respectively. Hallucinogens were more common at the trance night, and included substances such as THC, LSD, ketamine, DMT, and mescaline. This method allowed us to identify LSD on nine smartphone swabs (Supplementary Figure S1).

NPS were underreported and more frequently detected at the techno night. In this study, participants reported 2-CB (n=2), 3-MMC (n=2), and 1P-LSD (n=1) use. However, 10 swabs were positive for NPS. The participants did not report the use of ketamine derivatives (2F-DCK and DCK) or that of several entactogens (X-CMC, X-MMC, methylone, 5-MAPB).

Several medications, including psychoactive drugs, were identified: antidepressants (sertraline, mirtazapine, citalopram, and venlafaxine), anxiolytics (bromazepam oxazepam), hypnotics (zolpidem, doxylamine), painkillers (acetaminophen, tramadol), diphenhydramine, methylphenidate, diclofenac, and

Table 1: Consumption patterns and drugs identified on smartphone swabs of the two events.

	Overall (n=122)		Techno (n=61)		Trance (n=61)	
	n	%	n	%	n	%
Consumption patterns						
Drug consumption over smartphone	22	18.0	10	16.4	12	19.7
One substance declared	59	48.4	35	57.4	24	39.3
Two substances declared	50	41.0	25	41.0	25	41.0
Three or more substances declared	13	10.7	1	1.6	12	19.7
Drug identified on smartphone swabs						
MDMA	83	68.0	50	82.0	30	49.2
Cocaine	59	48.4	23	37.7	36	59.0
THC	51	41.8	23	37.7	28	45.9
Cocaine adulterants (lidocaine, phenacetine, levamisole)	30	24.6	12	19.7	18	29.5
Ketamine	22	18.0	6	9.8	16	26.2
Amphetamine	11	9.0	5	8.2	6	9.8
LSD	9	7.4	2	3.3	7	11.5
Methamphetamine	5	4.1	3	4.9	2	3.3
CBD	5	4.1	1	1.6	4	6.6
DMT	3	2.5	1	1.6	2	3.3
X-MMC	3	2.5	3	4.9	0	0.0
X-CMC	2	1.6	2	3.3	0	0.0
2F-DCK	2	1.6	2	3.3	0	0.0
DCK	2	1.6	0	0.0	2	3.3
2-CB	2	1.6	2	3.3	0	0.0
Heroin	1	0.8	0	0.0	1	1.6
5-MAPB	1	0.8	1	1.6	0	0.0
Methylone	1	0.8	1	1.6	0	0.0
Mescaline	1	0.8	0	0.0	1	1.6

MDMA, 3,4-methylenedioxy-N-methylamphétamine; THC, delta-9-tetrahydrocannabinol; LSD, lysergic acid diethylamide; CBD, cannabidiol; DMT, N,N-dimethyltryptamine; MMC, methylmethcathinone; CMC, chloromethcathinone; 2F-DCK, 2-fluorodeschloroketamine; DCK, deschloroketamine; 2-CB, 4-bromo-2,5-dimethoxyphenylethylamine; 5-MAPB, 1-(benzofuran-5-yl)-N-methylpropan-2-amine.

chloroquine. The participants reported most of them. Two participants reported using poppers, but these substances were not part of the targeted screenings. Three participants reported using magic mushrooms, but no psilocin or psilocybin was identified on the smartphone swabs. No participants reported GHB use.

Substance associations by night are presented in Figure 1. Visually, the distribution of drug associations was different for the two events. Indeed, the main substance associations identified were MDMA, as the central node, with NPS, cocaine, THC, and medications on night 1 (superior to 15 associations each). Because of the higher number of poly-drug users on night 2, a larger number of associations were identified. Interestingly, a higher number of associations were identified between ketamine and cocaine, as well as with LSD.

Smartphone swab test performance

The test performance based on reported drug use of participants is presented in Table 2, with the sensitivity, specificity, PPV, and NPV for cocaine, MDMA, THC, ketamine, and LSD. The sensitivity was >90 % for cocaine and MDMA but lower for THC, LSD, and ketamine. Specificity was >70 % for the five substances, suggesting a contamination issue with the smartphones.

In this method, metabolites of cocaine (benzoylecgonine, methylecgonine, and norcocaine), ketamine (norketamine), and MDMA (MDA) were screened to discriminate active use from contamination. In addition, we attempted to determine a cut-off mass spectrometry signal for cocaine, ketamine, and MDMA due to potential environmental contamination. We

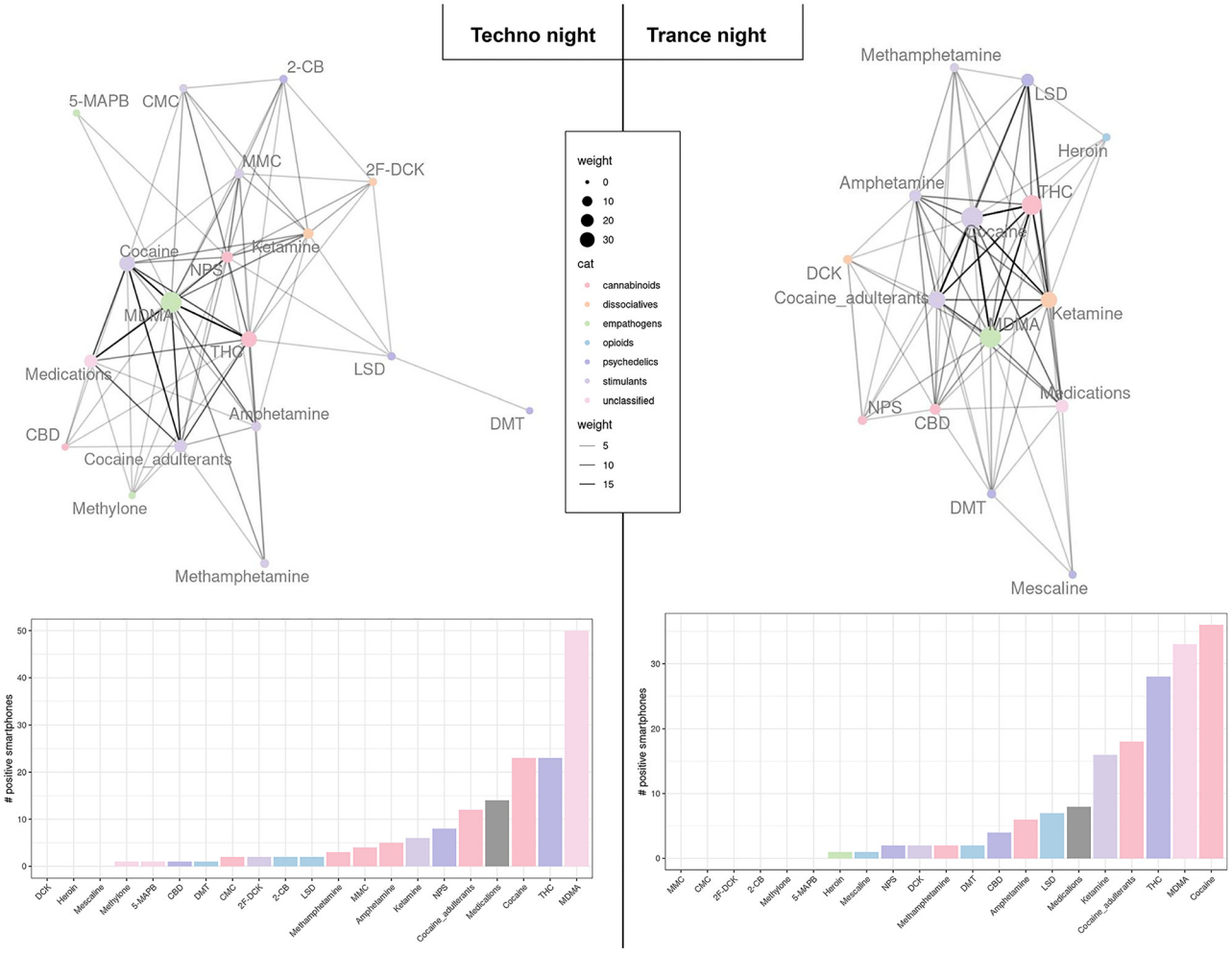

Figure 1: Network representation of drug associations for the two events. Drugs associations for each events are represented with networks, the line and their thickness represents the number of associations observed. Each dot represent a substance and their color are linked to their pharmacological class. Histograms show the number of positive smartphone per substance identified each night.

Table 2: Test performance for MDMA, cocaine, THC, ketamine, and LSD.

	MDMA	Cocaine	THC	Ketamine	LSD
Sensitivity, %	97.2	92.7	73.0	60	57.1
Specificity, %	72.0	88.1	71.8	85.7	99.0
Positive predictive value, %	83.3	86.4	52.9	27.2	88.9
Negative predictive value, %	94.7	93.6	85.9	96	94.7

MDMA, 3,4-methylenedioxy-N-methylamphétamine; LSD, lysergic acid diethylamide.

performed a ROC curve analysis, regardless of the presence of metabolites, with the declaration of the participants as the gold standard. The distributions of the normalized signals for cocaine, ketamine, and MDMA by haloperidol-d4 (IS), sorted by reported use or not, are presented in Figure 2. The test performance did not improve for MDMA or cocaine with a signal cut-off of 3.39 (Youden's index: 0.437, sensitivity: 91.8 %, specificity: 52 %) or 10.65 (Youden's index: 0.645, sensitivity: 87.3 %, specificity: 77.3 %). The performance for ketamine improved with a signal cut-off of 104.7 (Youden's index: 0.738, sensitivity: 80 %, specificity: 93.7 %). Thus, the identification of metabolites to confirm active use must be evaluated for each substance.

Discussion

This proof-of-concept study illustrates the potential of smartphone swab analysis in toxicology. It was possible to identify drugs of abuse, NPS, and medications, with their associated metabolites for certain substances using a highly sensitive UPLC-MS/MS method to detect traces of xenobiotics deposited by fingerprints on smartphone surfaces, as well as residual powder.

MDMA, cocaine, and THC, which are often identified as the most prevalent drugs in similar settings, were the most highly detected in our study. Indeed, Palamar et al. showed cocaine and ketamine to be the most highly used drugs in New York City by hair testing [24]. In Oslo, Norway, cocaine and THC were the most prevalent substances identified in the oral fluid of nightclub patrons [25]. In six Norwegian music festivals, cannabis, cocaine, and MDMA were also found to be the most prevalent substances using a combined approach [26]. No GHB use was reported in our population, even though its recreational use as a party drug has been reported for nearly three decades [27].

It is known that dance music fans who attend nightclubs are more likely to be prolific polydrug users [28]. In France, a study observed frequent polysubstance use by festival attendees [20]. Interestingly, this study identified the mix of cocaine and ketamine, known as the Calvin Klein mix [29]. The association of cocaine with ketamine has already been observed in France by hair testing in a high-risk population [30]. LSD was also mainly associated with ketamine and cocaine, suggesting a use pattern in our targeted population.

In our study, NPS use was underreported. The participants did not report the use of ketamine derivatives (2F-DCK and DCK) or several entactogens (X-CMC, X-MMC,

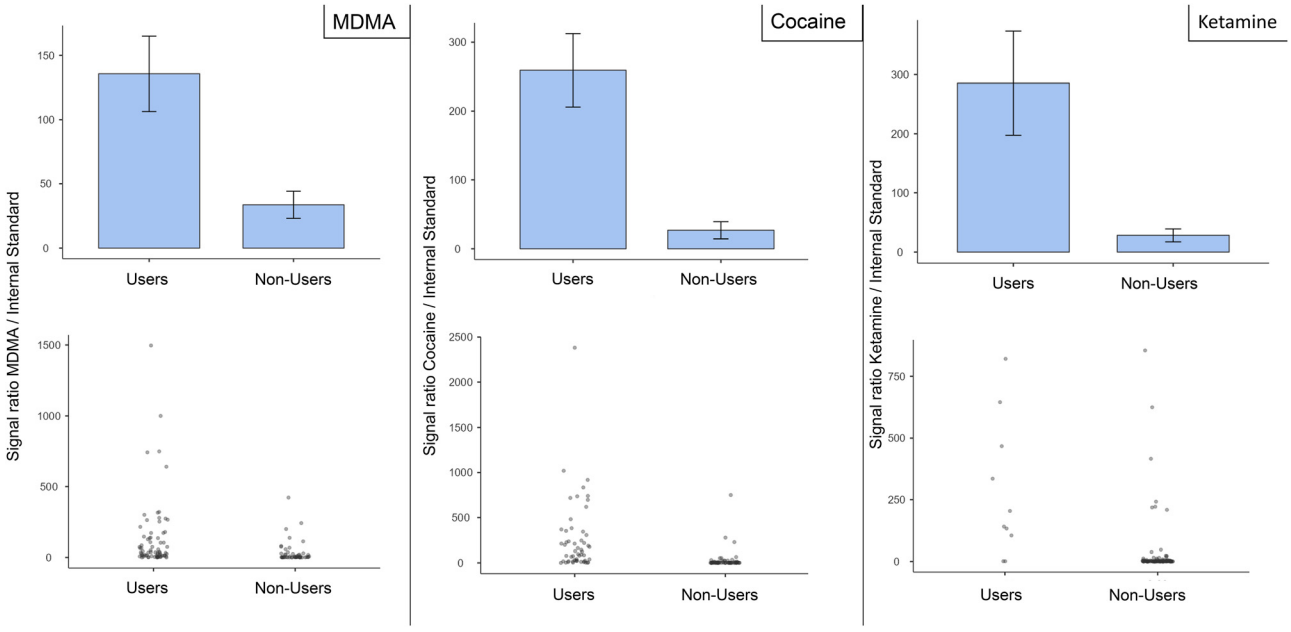

Figure 2: Normalized signal distribution of MDMA, ketamine, and cocaine between reported use and no reported use. Boxplot and individual dot representations of normalized mass spectrometry signals for MDMA, cocaine and ketamine from users and non-users based reported drug used.

methylone, and 5-MAPB). These NPS can be sold as ketamine or ecstasy pills and the exact substance is not known until analysis. A drug checking study identified novel dissociatives instead of ketamine in 30 % of the supposed ketamine samples in Australia [31]. This could explain the low sensitivity of smartphone swabs for ketamine in this context of uncontrolled products. Using hair analysis to detect drug exposure compared to reported use in USA, an estimated 43.8 % of participants tested positive for at least one drug after not reporting use [32]. In our study, the prevalence of NPS use was 10.7 %, higher than that reported in previous studies of 6.1 % based on reported use data [20] or oral fluid testing of drivers near a music festival (5.2 %) [33]. The ChEck iT! team showed that the intentional use of NPS in recreational settings is rare and that young people tend to use MDMA and amphetamines, as these substances are more easily available [13]. Thus, toxicology testing is important for evaluating the prevalence and trends of NPS use because of underreporting.

In our study, parent compounds predominated over metabolites in the fingerprints, which has been already observed by Adamowicz et al. [34].

Drug use patterns and substances were different in this study between trance and techno music night in club. Different drug use patterns have been already identified between rock festivals and clubs in Belgium, with more drug use in club [35]. For example, polydrug use was more frequent in trance music event than techno event, with more hallucinogens consumption. It is in accordance with *Karjanova* et al. study in Czech, concluding that hallucinogens occupy a dominant place in the psychedelic trance subculture and cocaine is tolerated drug [36]. Conversely, MDMA was the most identified drug is the techno night, suggesting different use patterns between the two populations. It has been shown that MDMA use was correlated to music, dance and excite when asking attendance motive in EDM events in Belgium [37]. Those findings suggest that toxicology screenings should be adapted when music type is known for intoxicated patient in club, festival or more electronic music events, with a focus on hallucinogens for trance music events.

Strengths of the study

The main strengths of this method are that it is easily scalable in the field and provides information on individual consumption. Because of the use of a dry swab, this study was well accepted by users. Other advantages of the method are that there is no need of trained staff for sampling and the procedure is inexpensive (9 cents per swab). This approach is suited for festival or nightclub events beacause sampling is very fast (20 s), in particular in the context of harm-reduction programs or toxico-epidemiolgy studies.

This approach provides a complementary tool to oral fluid analysis, wastewater analysis, in-the-field drug checking, and declarative data for drug testing in toxico-epidemiology.

Another strength of this study was the study population, consisting of nightclub goers using drugs, who are difficult to reach in field research. It should be noted that the size of the study population was moderate (122 participants from over 2000 attendees).

Limitations of the study

As this study was declarative, the data collected depended on the quality of the interview and the reliability of the declarant. The use of psychoactive substances by the participants before data collection likely led them to forget information or make errors. The lack of correspondence between the substances sold and the actual content of the products was also likely to have increased false negative results, which has already been described for 3-MMC users [38] and nightclub attendees [24]. Declaration of a substance could also have been biased by the seller and thus may have distorted the results of the study. Finally, it is also possible that the phone was touched by or used as a consumption surface by a third person but not reported [9, 39].

Another limitation of this study was that high-resolution mass spectrometry was not used. Indeed, this technology is particularly useful for the identification of unknown compounds [40]. It cannot be ruled out that new NPS that were not part of our libraries could have been used.

In addition, substance stability on smartphones should be studied. Certain substances can be detected in fingerprints up to 20 days after consumption, such as sertraline or hydroxyzine [34]. Furthermore, it was possible to detect diphenhydramine and scopolamine on a smartphone15 days after intake [11]. In this study, we ask the participants to report their drug consumption over the last seven days, which could explain a certain number of false positives.

An appropriate design, with a wide range of cases and controls, and the avoidance of bias and confounding factors are necessary to obtain valid and reliable conclusions when evaluating the performance of diagnostic tests [41]. Thus, our results of the ROC analysis should be interpreted with caution.

Conclusions

This proof-of-concept study of 122 subjects shows that smartphone-swab analysis could provide a useful and complementary tool in drug testing, with acceptable test performance, despite the use of declarative data. It was possible

to identify drugs of abuse, NPS, and medications, with their associated metabolites for certain substances. The advantages of this method are the use a dry swab, a quick sampling procedure, and the use of widely accessible tandem-mass spectrometry. Although this method has several limitations, as discussed, this new alternative matrix is promising for harm-reduction programs and toxico-epidemiolgy studies.

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Research ethics: This project is a research project that does not involve the human being and whose controller is the Centre Hospitalier Grenoble-Alpes. This research has been registered in accordance with French regulations and meets the requirements of the CNIL reference methodology (HDH: F20231117141629).

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: The authors states no conflict of interest.

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Data availability: Not applicable.

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